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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,417	12/22/2004	Patrick Cornelis Nicolaas Rensen	101137-60	7547

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
08/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,417	RENSEN ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-20 and 22-33* is/are pending in the application.

4a) Of the above claim(s) *19,20,29 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,18,22-28 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The In view of the Appeal Brief filed on March 18, 2009, PROSECUTION IS HEREBY REOPENED. For the reasons set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

Amendment Entry

2. The amendment of November 24, 2009 has been entered. Claims 1-16 are cancelled. Claims 19-20, 29 and 33 are withdrawn. Claims 17-18, 22-28 and 30-32 are under consideration in this office action.

Withdrawal of Rejections

3. The following objections and rejection are withdrawn in view of applicants' amendments and arguments:

a) The rejection of claims 17-18, 22-28 and 30-32 under 35 U.S.C. 112, second paragraph;

b) The rejection of claims 18, 22, 23, 25, 27-31 under 35 U.S.C. 102(b) as being anticipated by Quarfordt et al., J. of Biological Chem. 1982. Vol. 257(24): 14642-14647; and

c) The rejection of claims 17-18 and 22-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oosten et al., (J. of Biol. Chem. 2001. Vol. 276(23): 8820-8824) in view of Quarfordt et al., (J. of Biological Chem. 1982. Vol. 257(24): 14642-14647).

Previous Grounds of Objection

Claim Objections

4. Claims 17 and 32 are objected to because of the following informalities: Claim 32 depends upon itself. It appears that no amendments has been made to claim 32, therefore appropriate correction is required. Furthermore, claims 17 and 32 are both drawn to the mammal being a human, therefore it appears that the claims maybe repetitive. Thus, appropriate clarification is required.

Response to Arguments

5. Applicant's arguments with respect to claims 17-18, 22-28 and 30-32 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 17-18, 22-28 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dasseux et al., (WO 99/16458 published April 8, 1999) in view of Rozek et al., (Biochemistry. 1995. Vol. 34, pages 7401-7408).

Claim 27 is drawn to a method for treating a mammal suffering from or is at risk of developing sepsis or septic shock comprising administering to such mammal a therapeutically effective amount of a peptide and pharmaceutically acceptably adjuvants where the peptide comprises an amino acid sequence selected from SEQ ID NO:11, SEQ ID NO:2 and SEQ ID NO:1. Claim 28 is drawn to the peptide comprising SEQ ID NO: 1. Claim 30 is drawn to the peptide comprising SEQ ID NO:2. Claim 31 is drawn to the peptide being the amino acid sequence of SEQ ID NO:2.

Claims 17 and 32 are drawn to the mammal being a human. Claim 18 is drawn to the mammal being at an increased risk of developing sepsis. Claim 22 is drawn to the peptide binding to lipoteichoic acids and wherein the composition is for preventing or treating a sepsis or septic shock in mammals. Claim 23 is drawn to the shock being caused by Gram-negative bacteria. Claims 24 and 26 are drawn to the mammal being a human, horse, cow, dog or cat. Claim 25 is drawn to the shock being caused by the shock is caused by Gram-positive bacteria.

Dasseux et al, teach apolipoprotein A-1 agonist compositions for treating disorders such as septic shock (page 1, lines 5-9). Dasseux et al, teach the desire to mimic the activity ApoA-I with specific activities such as activation of LCAT approaching that of the native molecule (page 17, lines 17-21). Dasseux et al, teach the ApoA-I agonist are peptides that form amphipathic helices in the presence of lipids, bind lipids, form pre-B-like or HDL-like complexes, activate LCAT, increase serum levels of HDL fractions and promote cholesterol efflux (page 17, lines 20-27). Dasseux et al, teach the peptide design is based on the helical structure and amphipathic properties of 22 amino acid consensus sequence derived from the helical repeats of ApoA-I (page 17, lines 28-32). Dasseux et al, teach the having negative charges being distributed on the rest of the hydrophilic face of the peptide (page 33, lines 25-29). Dasseux et al, the agonist can be used to treat any animals, especially mammals, including humans for enotoxemia which results in septic shock (page 78, lines 9-20). It is noted that sources of sepsis or septic shock can be caused by gram-negative or gram-positive bacteria. Dasseux et al, teach administering the peptide by any suitable route to ensure

bioavailability (page 83, lines 30-36) and pharmaceutical formulations including a wide variety of pharmaceutically acceptable adjuvant carriers (page 76, lines 24-32). However Dasseux et al, do not teach administering SEQ ID NO:1, 2 or 11.

Rozek et al., teach apolipoprotein C-I (ApoC-I) is an exchangeable apolipoprotein distributed mainly in HDL and VLDL, where HDL facilitates the uptakes of cholesterol (page 1858, col.1). Rozek et al., teach that LCAT is primarily activated by ApoA-I, whereas ApoC-I serves as the secondary activator and stimulates LCAT activity up to 78% as effectively as ApoA-I (page 1858, col.2). Rozek et al., teach ApoA-I having affinity for lipids (page 1859, col.1). The main structural motif which facilitates the interaction of the exchangeable apolipoprotein with lipids is the amiphipathic helix which is defined as an a-helix with opposing polar and nonpolar faces (page 1859, col.1). Rozek et al., notes that Rozek et al., (Biochemistry 1995, Vol. 34:7401-7408) disclose peptides corresponding to the lipid binding domain of apoC-I and is characterized by repeating amino acid motifs of 22 resides which form the amphipathic helical structure when associated with lipids (Rozek et al., (Biochemistry 1995, Vol. 34:7401). Furthermore ApoC-I directly increases HDL serum levels. Rozek et al., teach the hydrophobic side chains are exclusively on the concave face, forming two hydrophobic clusters; there are positively charged side chains at the interface of the peptide and the negatively charged side chains are located on the hydrophilic face of the molecules (page 1863-4, col.2-2). Furthermore, Rozek et al., disclose peptides comprising amino acid sequences from SEQ ID NO:11, 2 and 1.

Therefore it would have been prima facie obvious at the time of applicants' invention to apply the peptide comprising the amino acid sequence as taught by Rozek et al., into the method for treating a mammal suffering from or is at risk of developing sepsis or septic shock comprising administering a therapeutically effectively amount of a peptide and pharmaceutically acceptably adjuvants as taught by Dasseux et al., in order to provide an apolipoprotein A-I agonist composition for treating endotoxemia or septic shock. One of ordinary skill in the art would have a reasonable expectation of success by including ApoC-I peptide within the composition of method of treating sepsis or shock because the art teaches the using peptides that mimic the activity ApoA-I such as activation of LCAT and Rozek et al., teach the ApoC-I peptide has said ability. Furthermore, no more than routine skill would have been required to include the ApoC-I peptide because Rozek et al., teach that the ApoC-I peptide forms amphipathic helices in the presence of lipids, bind lipids with its lipid binding domains, increases serum levels of HDL fractions and promotes cholesterol efflux, just as required of an ApoA-I agonist. Finally all of the claimed elements, such as peptides that qualify as ApoA-1 agonist and peptides comprising SEQ ID NO:1, 2, or 11, were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

7. Claims 17-18, 22-28 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dasseux et al., (US Patent 6,004,925 published December 21, 1999) in view of Rozek et al., (Biochemistry. 1995. Vol. 34, pages 7401-7408).

Claim 27 is drawn to a method for treating a mammal suffering from or is at risk of developing sepsis or septic shock comprising administering to such mammal a therapeutically effective amount of a peptide and pharmaceutically acceptably adjuvants where the peptide comprises an amino acid sequence selected from SEQ ID NO:11, SEQ ID NO:2 and SEQ ID NO:1. Claim 28 is drawn to the peptide comprising SEQ ID NO: 1. Claim 30 is drawn to the peptide comprising SEQ ID NO:2. Claim 31 is drawn to the peptide being the amino acid sequence of SEQ ID NO:2.

Claims 17 and 32 are drawn to the mammal being a human. Claim 18 is drawn to the mammal being at an increased risk of developing sepsis. Claim 22 is drawn to the peptide binding to lipoteichoic acids and wherein the composition is for preventing or treating a sepsis or septic shock in mammals. Claim 23 is drawn to the shock being caused by Gram-negative bacteria. Claims 24 and 26 are drawn to the mammal being a human, horse, cow, dog or cat. Claim 25 is drawn to the shock being caused by the shock is caused by Gram-positive bacteria.

Dasseux et al, teach apolipoprotein A-1 agonist compositions for treating disorders such as septic shock (col. 2, lines 55-5). Dasseux et al, teach the desire to mimic the activity ApoA-I with specific activities such as activation of LCAT approaching that of the native molecule (col. 11, lines 50-55). Dasseux et al, teach the ApoA-I agonist are peptides that form amphipathic helices in the presence of lipids, bind lipids,

form pre-B-like or HDL-like complexes, activate LCAT, increase serum levels of HDL fractions and promote cholesterol efflux (col. 11, lines 55-60). Dasseux et al, teach the peptide design is based on the helical structure and amphipathic properties of 22 amino acid consensus sequence derived from the helical repeats of ApoA-I (col.11, lines 61-67). Dasseux et al, teach the having negative charges being distributed on the rest of the hydrophilic face of the peptide (col. 20 lines 48-53). Dasseux et al., teach pharmaceutical formulations containing ApoA-I agonist and their use to treat diseases associated with endotoxemia, i.e., septic shock (col. 12, lines 14-21).Dasseux et al, the agonist can be used to treat any animals, especially mammals, including humans for enotoxemia which results in septic shock (col. 49, lines 47-59). It is noted that sources of sepsis or septic shock can be caused by gram-negative or gram-positive bacteria. Dasseux et al, teach administering the peptide by any suitable route to ensure bioavailability (col. 52, lines 46-67) and pharmaceutical formulations including a wide variety of pharmaceutically acceptable adjuvant carriers (col. 48, lines 59-68). However Dasseux et al, do not teach administering SEQ ID NO:1, 2 or 11.

Rozek et al., teach apolipoprotein C-I (ApoC-I) is an exchangeable apolipoprotein distributed mainly in HDL and VLDL, where HDL facilitates the uptakes of cholesterol (page 1858, col.1). Rozek et al., teach that LCAT is primarily activated by ApoA-I, whereas ApoC-I serves as the secondary activator and stimulates LCAT activity up to 78% as effectively as ApoA-I (page 1858, col.2). Rozek et al., teach ApoA-I having affinity for lipids (page 1859, col.1). The main structural motif which facilitates the interaction of the exchangeable apolipoprotein with lipids is the amiphipathic helix which

is defined as an a-helix with opposing polar and nonpolar faces (page 1859, col.1). Rozek et al., notes that Rozek et al., (Biochemistry 1995, Vol. 34:7401-7408) disclose peptides corresponding to the lipid binding domain of apoC-I and is characterized by repeating amino acid motifs of 22 resides which form the amphipathic helical structure when associated with lipids (Rozek et al., (Biochemistry 1995, Vol. 34:7401). Furthermore ApoC-I directly increases HDL serum levels. Rozek et al., teach the hydrophobic side chains are exclusively on the concave face, forming two hydrophobic clusters; there are positively charged side chains at the interface of the peptide and the negatively charged side chains are located on the hydrophilic face of the molecules (page 1863-4, col.2-2). Furthermore, Rozek et al., disclose peptides comprising amino acid sequences from SEQ ID NO:11, 2 and 1.

Therefore it would have been prima facie obvious at the time of applicants' invention to apply the peptide comprising the amino acid sequence as taught by Rozek et al., into the method for treating a mammal suffering from or is at risk of developing sepsis or septic shock comprising administering a therapeutically effectively amount of a peptide and pharmaceutically acceptably adjuvants as taught by Dasseux et al., in order to provide an apolipoprotein A-I agonist composition for treating endotoxemia or septic shock. One of ordinary skill in the art would have a reasonable expectation of success by including ApoC-I peptide within the composition of method of treating sepsis or shock because the art teaches the using peptides that mimic the activity ApoA-I such as activation of LCAT and Rozek et al., teach the ApoC-I peptide has said ability. Furthermore, no more than routine skill would have been required to include the ApoC-I

peptide because Rozek et al., teach that the ApoC-I peptide forms amphipathic helices in the presence of lipids, bind lipids with its lipid binding domains, increases serum levels of HDL fractions and promotes cholesterol efflux, just as required of an ApoA-I agonist. Finally all of the claimed elements, such as peptides that qualify as ApoA-1 agonist and peptides comprising SEQ ID NO:1, 2, or 11, were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Conclusion

8. No claims allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645